Original Paper

Cardiac Hemodynamics and Slight Regression of Left Ventricular Mass Index in a Group of Hemodialysed Patients

DANIELA-TEODORA MARIA[1], ALEXANDRU ANDRITOIU[2], CRISTINA VADUVA[3], KAMAL CONSTANTIN KAMAL[4], SORIN IOAN ZAHARIE[1]

[1]Nephrology Department, Clinical Emergency County Hospital Craiova, University of Medicine and Pharmacy of Craiova

[2]Internal Medicine Department, Clinical Military Hospital Craiova

[3]Hemodialysis Center-Nephrology Department, Clinical Emergency County Hospital Craiova, University of Medicine and Pharmacy of Craiova, Nephrology Department, Clinical Emergency County Hospital Craiova

[4]Department of Family Medicine, University of Medicine and Pharmacy of Craiova

ABSTRACT: Chronic kidney disease (CKD) is a major health problem and has a growing prevalence in Romania and worldwide. The concept of chronic kidney disease (CKD) is defined by abnormal kidney function and/or structure persisting for more than 3 months, influencing patients health. Patients with chronic kidney disease have a 20-30 times greater risk for cardiovascular morbidity and mortality than similar individuals without chronic kidney disease. We conducted a prospective observational study that included 33 patients on hemodialysis. All patients were performing hemodialysis for at least 6 months, 3 sessions per week at a private Haemodialysis Centre in Craiova. Left ventricular hypertrophy has a high prevalence in dialysis patients and increased left ventricular mass index (LVMI) is a major cardiovascular risk factor. We concluded that concentric and eccentric ventricular hypertrophy are present simultaneously in hemodialysis patients, LVH regression is possible, but requires an interventional approach on cardiovascular risk factors (anemia, blood pressure, secondary hyperparathyroidism) in hemodialysis patients, patients on dialysis with a higher fistula flow, over 1170ml/min have heart failure, and the fistula's constant increased flow is a risk factor for heart failure with a high flow.

KEYWORDS: *Chronic kidney disease (CKD), Left ventricular hypertrophy, Left ventricular mass index (LVMI), hemodialysis.*

Introduction

Chronic kidney disease (CKD) is a major health problem and has a growing prevalence in Romania and worldwide.

The concept of chronic kidney disease (CKD) is defined by abnormal kidney function and/or structure persisting for more than 3 months, influencing patients health [1].

NHANES study (2005-2010) revealed a prevalence of 13.1% for patients with stages 3 and 4 CKD in the USA, and 8.5% prevalence of heart failure [2].

In Australia, AusDiab study revealed a prevalence of 4.8% for patients with glomerular filtration rate below 60ml/min/1.73m2 between 2011-2012 [3].

People with CKD are at risk of developing end-stage renal disease requiring transplant or other renal replacement therapies.

In Romania there has been a rise in dialysis patients from 5800 in 2003 to 10,470 at the end of 2012 [4].

Patients with chronic kidney disease have a 20-30 times greater risk for cardiovascular morbidity and mortality than similar individuals without chronic kidney disease [2,5-8].

Increased cardiovascular risk is due to high prevalence of traditional and non-traditional (urea own factors) cardiovascular risk factors.

Approximately 15% of CKD patients starting dialysis have left ventricular systolic dysfunction [9].

Important epidemiological and interventional trials conducted in healthy population revealed that certain risk factors are associated with an increased rate of cardiovascular events.

Same risk factors are reproducible in patients with renal impairment (Table 1).

Table 1. Cardiovascular risk factors in CKD patients.

Traditional risk factors	Uraemia specific risk factors	Dialysis related risk factors
Age	Hemodynamic overload	
Sex-male	Secondary hyperparathyroidism	Blood presure fluctuations
High blood presure	Anemia	Electrolyte fluctuations
Diabetes	Hypoalbuminemia	**Arterio-venous fistula**
Hyperlipidemia	High fibrinogen	Dialysis substance impurity
Obesity	Hyperhomocysteinemia	Incompatibility
Menopause	Dyslipoproteinemia	Changes of cardiac filling during dialysis or during the inter-dialytic interval
Smoking	Resistance to insulin	
Inactivity	Increased Ca x P	
	Metabolic acidosis	
	Chronic inflammatory condition	
	Oxidative stress	
	Carbonyl stress	

After: Ursea N, Chronic renal failure, Nephrology, II nd edition, vol. I,
Romanian Kidney Foundation Publishing House, 2006

Table 2. Local and general hemodynamics changes due to AVF creation.

Local hemodynamic disturbances	General hemodynamic disturbances
venous hypertension with turgid draining veins	decrease in mean arterial pressure by reducing peripheral resistance heart
venous arterialization	increased preload to the right
increase in venous oxygen saturation at 94-98%	increased heart rate
occurrence of turbulence phenomena expressed by thrill and bruit	increased cardiac output

After Ursea N and al. Artificial kidneyand other means for extrarenal epuration.
Romanian Kidney Foundation Publishing House, 39-147, 1997

Permanent vascular access is essential to perform adequate hemodialysis in uraemic patients.

Creation of permanent vascular access, represented by AVF, produces local and general changes in normal hemodynamics (Table 2).

The long-term effects of hemodialysis arteriovenous fistula (AVF) to cardiac hemodynamics creates controversy especially in patients on dialysis for more than 6 months.

The volume and pressure overload act synergistically resulting in ventricular hypertrophy in patients with end-stage renal disease (ESRD).

Serial echocardiographic monitoring of dialysis patients can provide useful information in detection of cardiac changes that may result in adverse cardiovascular events.

Doppler ultrasound evaluation of the vascular bed prior to the arteriovenous fistula placement should be required to make a successful vascular access, as well as maturing and evolving.

We aimed to evaluate echocardiographic changes in a group of hemodialysis patients and assess by Doppler sonography relationships between the fistulas flow and cardiac output.

Materials and Method

Between February 1, 2014 and August 15th 2014, we conducted a prospective observational study that included 33 patients on hemodialysis.

All patients were performing hemodialysis for at least 6 months, 3 sessions per week at a Private Haemodialysis Centre in Craiova.

Permanent vascular access had 3 locations: radio-cephalic (Group A), brahio-cephalic (Group B) and brahio-basilica (Group C).

All patients were evaluated by standard 2-D, M-mode and Doppler cardiac and AVF ultrasound.

We used a Siemens Sonoline Prima SLC device in the Internal Medicine Clinic of Military Emergency "Dr. Stefan Odobleja" Craiova Hospital.

Echocardiographic and vascular access measurements were performed in accordance with the recommendations of the American Society of Ecocardiography (ASE) [10] by an experienced investigator (A.A.) with competence in vascular and cardiovascular ultrasound.

The target echocardiographic parameters were LV diameters in systole and diastole,

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LVMi, LVVi, RWT, wave E, wave A to which is added EF calculated with Simpson method.

Regarding Doppler evaluation of FAV, this was done mid-week, between 2 hemodialysis sessions, and the parameters that were analyzed are: PI (pulsatility index), RI (resistivity index), PSV (peak systolic velocity), MDV (medium diastolic velocity), TAMX (time averaged maximum velocity), TAV (time averaged mean velocity), area and diameter of blood vessel as well as Fvol flow volume (Figure 1 and Figure 2).

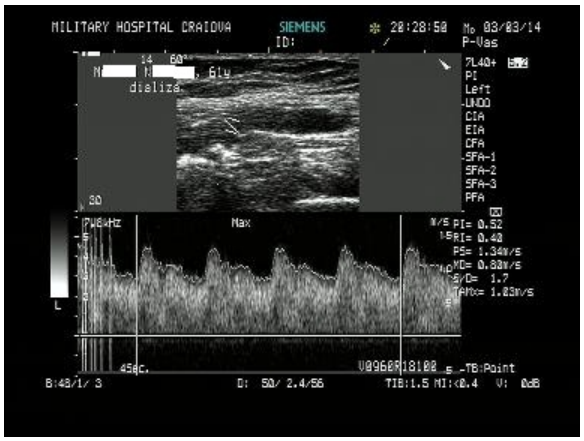

Figure 1. Doppler ultrasound of Radial artery.

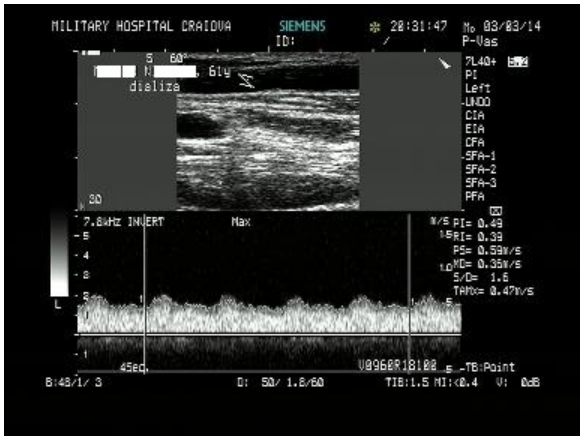

Figure 2. Doppler ultrasound of Cephalic vein.

Cardiovascular risk at 10 years of major cardiovascular event (acute myocardial infarction or stroke) was calculated using QRISK2.

Blood tests have been performed including: predialysis and post-dialysis serum urea, creatinine, Hb, total cholesterol, HDL-cholesterol, Serum calcium, Serum phosphorus, iPTH, total iron binding capacity (TIBC), Serum iron, Alkaline phosphatase and Albumin.

Results

There were 17 women and 16 men, mean age 49.64±15.72 years.

The average duration of renal replacement therapy from the onset and until inclusion in the study was 29.30±15.84 months.

There were no statistically significant differences between the 3 types of fistulas average duration, although radio-cephalic and brahio-cephalic fistuls had a longer duration of use.

Comparative analysis of clinical, laboratory and ultrasound parameters at baseline according to the distribution of the groups

There were no statistically significant differences in terms of age, systolic or diastolic blood pressure, presence of hypertension or diabetes, but the prevalence of females is remarkable both in the overall group, as well as lots brahiocephalic and brahiobasilic fistula (p=0.009).

-IVS (interventricular septum) and PWT(posterior wall thickness of left ventricle) were significantly higher in patients with radiocephalic fistula vs those with brahiobasilic fistula (p=0.015). The volume index of LV (LVVi) was significantly higher in patients with brahiocephalic fistula vs those with radio-cephalic and brahiobasilic fistulas (p=0.048).

-Overall prevalence of LVH at time 0 was 55% and concentric LVH predominated (43%). Normal LV geometry had 36% of patients and 12% of them had eccentric LVH. Pressure and volume overload are acting on dialysis patients and I noticed that the ejection fraction and SBP are factors of LVH progression.

-LV dilation expressed as the LVVi >90g/m^2 was present in 18% of patients at baseline. Diastolic dysfunction represented by the ratio E/A<1 was present in 58% of patients at baseline.

-A percentage of 36% of patients had heart failure. Fistula's venous flow was significantly higher (p<0.001) in patients with heart failure than in patients without heart failure (Figure 3).

I wanted to know fistula's flow threshold from which heart failure occurs. This value is 1170, with Sn (85.71%) and Sp (80.0%), representing a viable threshold to discern between patients with or without heart failure (Figure 4, Table 3).

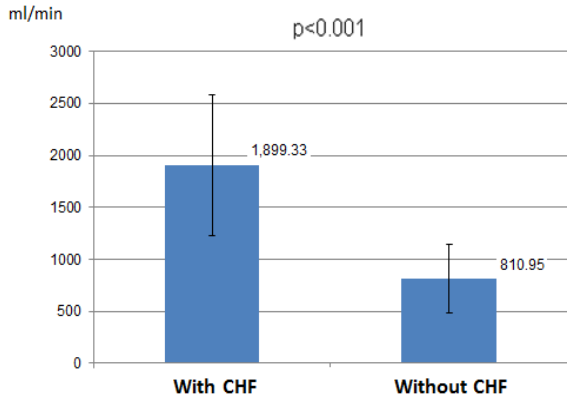

Figure 3. Mean AVF venous flow in CHF patients.

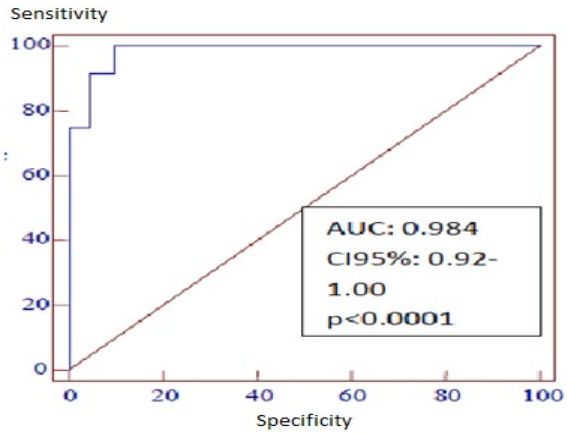

Figure 4. ROC curve analysis for threshold of AVF flow volume predictor of CHF.

Table 3. Parameters obtainen for the ROC curve analysis.

AVF flow volume	Sensibility	Specificity	VPP	VPN	LR+	LR-	Sn+Sp
1160	100.00%	85.71%	80.00%	100.00%	7	0	185.71%
1170	100.00%	90.48%	85.71%	100.00%	10.5	0	190.48%
1200	91.67%	90.48%	84.62%	95.00%	9.63	0.09	182.14%

Comparative analysis of clinical, laboratory and ultrasound parametres at visit 1 according to the group distribution

In patients with brahiobasilic fistula, PWT and IVS were higher than those with radio-cephalic fistula (p=0.047). In patients with brahiocephalic fistula, LVVi was higher than patients in the other two groups (p=0.041). Mitral A velocity was higher in patients with brahiocephalic fistula than those with brahiobasilic and radiocephalic fistulas (p=0.008).

There were statistically significant differences between fistula's flow ultrasound parameters through the artery and the vein:

-PI of the vein was higher in patients with brahiocephalic fistula vs. radiocephalic fistula patients (p=0.046);

-PSV from the vein was lower in patients with radiocephalic fistula vs. brahiocephalic and brahiobasilic fistulas (p=0.002);

-TAMX and MDV of vein were higher in patients with brahiobasilic fistula vs. brahiocephalic and radiocephalic fistulas (p<0.0001 and p=0.002).

It was observed that ejection fraction and shortening fraction are factors of progression of LVH.

Comparative analysis of clinical, laboratory and ultrasound parameters at visit 2 depending on group distribution

Notably, at the time of the final evaluation, after six months from the time of enrollment, paraclinical parameters revealed the following situations:

-IVS and PWT were lower in patients with brahiobasilic fistula to those radiocephalic fistula (p=0.011); LVMI was lower in patients with brahiobasilic fistula to patients with radiocephalic and brahiocephalic fistulas (p=0.016 and p=0.006);

-ejection fraction and shortening fraction of LV are lower in patients with brahiocephalic fistula vs. patients with radiocephalic fistula (p=0.006 and p=0.003);

-vein PSV, MDV and TAMX are higher in patients with radiocephalic fistula vs brahiobasilic and brahiocephalic fistulas;

-veins flow volume was lower in patients with radiocephalic fistula vs. brahiocephalic and brahiobasilic fistula (p=0.004, p=0.043);

-PSV, MDV, TAMX, TAV and Fvol of the artery were significantly lower in patients with radiocephalic fistula vs. brahiobasilic and brahiocephalic fistula.

It was observed that cardiac output, ejection fraction and shortening fraction are factors of progression of LVH.

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Comparative analysis of clinical, laboratory and ultrasound findings in dynamic

Although several variables have an up or down trend, statistically significant differences were only for resistivity index (RI) in the vein, which increases progressively with time and that DBP decreases gradually with time. The increase in the IR means an increased resistance to blood flow at the periphery. We observed decrease in PSV and MDV but without statistical significance.

Mean hemoglobin values increased during monitoring (p=0.004), which shows a better management of anemia in dialysis patients. The mean serum albumin also increased.

Comparing the mean value of LVMi, we found a decrease in LVMi between baseline and visit 2, without statistical significance (p=0.819). LVVi also decreased during follow-up unfortunately with no statistically significant differences (p=0.555).

Diastolic dysfunction, represented by the average ratio E/A, has remained relatively constant. Both ejection fraction and shortening fraction of LV had an increasing trend over time, without statistical significance (Figure 5).

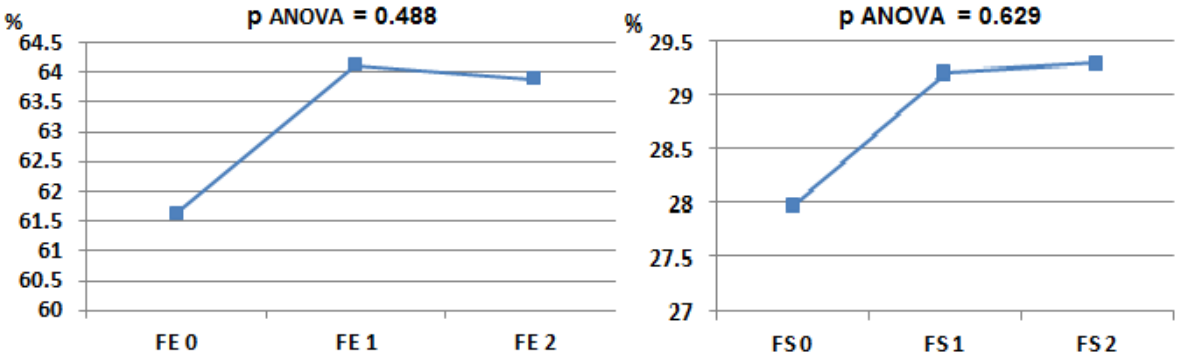

Figure 5. Dynamic analysis of cardiac ejection fraction and shortening fraction.

Cardiac output decreased during the 6 months of follow-up, but without statistical significance. Cardiac output was higher in patients with brahio-cephalic and radio-cephalic fistulas. Venous flow in the radiocephalic fistula was significantly lower than the other fistulas (p=0.0001) and had a discrete upward trend.

Statistically significant correlations between cardiac output and fistula's arterial flow were present only in patients with radiocephalic fistula.

Cardiovascular risk assessment using QRISK2-2014

We evaluated a link between cardiovascular risk estimated by QRISK2 and various cardiovascular risk factors present in patients with end-stage CKD, using Pearson correlation coefficient. The data obtained are shown in Table 4.

Table 4. Cardiovascular risk assessment using QRISK2.

Factor	r	p
Hb	0.234	0.189
Age	0.702	**<0.0001**
Col/HDL	0.829	**<0.0001**
iPTH	0.321	**0.053**
Post-dialysis ureea	0.415	**0.016**
LVMi	-0.153	0.392
LVVi	-0.029	0.871
E/A	-0.365	**0.036**
SBP	0.416	**0.016**
DBP	0.227	0.202
Cardiac output	0.359	**0.040**
Fvol vein	-0.097	0.590
Fvol artery	0.013	0.942

Discussion

Overall prevalence of LVH at baseline was 55%.

The concentric type of LVH was predominent (43%), but there was a fairly large group of patients with eccentric LVH (12%), so we can say that both pressure overload and volume overload are present in the study group.

According to Middelton et al. in patients with CKD on hemodialysis is better to estimate LVH by LV volume index (LVVi) and not using relative wall thickness (RWT) because it turned out that this can be estimated in a higher risk of cardiovascular morbidity and mortality [11].

LV dilation expressed as the LVVi>90g/m^2 was present in 18% of patients at baseline.

There are several mechanisms associated with LVH, which contribute to increased cardiovascular risk in patients with CKD.

LVH is associated with myocardial fibrosis and diastolic dysfunction, as a major factor in the development of heart failure.

In our study, diastolic dysfunction was present in 58% of patients at baseline and heart failure at 36% of patients.

Patients with heart failure had a fistula flow significantly higher than in patients without heart failure.

Fistula threshold value output for heart failure is 1170ml/min. In dialysis patients may appear high output cariac failure due to increased flow of vascular access.

Thus, a significant amount of arterial blood passes through the fistula into venous circulation and increases the preload, wich increases cardiac output.

As result, in time, volume overload produces cardiac hypertrophy, and on a heart with diastolic dysfunction, heart failure [12].

Currently, most of the literature argues that LVH in dialysis patient is irreversible, and any increase in LVMi is associated with increased risk of cardiovascular events in these patients [13].

However, in recent years, different studies showed a regress of LVH in dialysis over the years, through adequate control of anemia, prevention or control of hyperphosphatemia, hyperhydration and in patients after a transplant was performed [14,15].

In our study LVMi decreased over time, but this did not reach statistical significance.

A positive outcome in our study was the improvement of the ejection fraction and shortening fraction of LV, although not reaching statistical significance, the numerical differences are obvious. Probably a long period of follow-up would definitely be inclined to a positive balance.

Cardiac output decreases during the 6 months of follow-up, but was higher in patients with FAV brahiocephalic and radio-ephalic fistulas, than those with brahiobasilic fistula.

The results suggest that the reduction in cardiac output after hemodialysis is related to the redistribution of blood volume away from the heart.

Performing a correlation analysis between cardiac output and venous flow through the fistula, showed no statistically significant correlations were identified.

Statistically significant correlations between cardiac output and arterial flow were present only in patients with radio-cephalic fistula.

Throughout the study fistula's vein diameter and area were significantly lower in patients with radiocephalic fistula to brahiobasilic and brahiocephalic fistulas.

This together with the fact that the average flow for radiocephalic fistula was significantly lower than that of veins flows for brahiobasilic and brahiocephalic, betrays that vascular bed level 0 is smaller in size.

However there is no difference between the flow rate or the blood pulse wave parameters.

We evaluated a link between cardiovascular risk estimated by QRISK2 and various cardiovascular risk factors present in patients with end-stage CKD.

The age and the cholesterol/HDL-cholesterol ratio are strongly correlated with QRISK2.

The value of iPTH, post-dialysis urea, SBP and cardiac output correlates directly proportional to cardiovascular risk, while E/A correlated inversely with QRISK2.

Unfortunately there was no evidence of a correlation between arteriovenous fistula flow and cardiovascular risk, betraying this complex pathophysiology behind fistula's hemodynamics, and the need to assess in real-time, the risk of cardiovascular morbidity and mortality.

Conclusions

Left ventricular hypertrophy has a high prevalence in dialysis patients and increased LV mass index is a major cardiovascular risk factor.

Concentric and eccentric ventricular hypertrophy are present simultaneously in hemodialysis patients.

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LVH regression is possible, but requires an interventional approach on cardiovascular risk factors (anemia, blood pressure, secondary hyperparathyroidism) in hemodialysis patients.

Patients on dialysis with a higher fistula flow, over 1170ml/min have heart failure, and the fistula's constant increased flow is a risk factor for heart failure with a high flow.

Conflict of interests

None to declare.

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Corresponding Author: Kamal Constantin Kamal, Department of Family Medicine, University of Medicine and Pharmacy of Craiova, Petru Rares St., No.2, Craiova 200349; e-mail: kamalconstantin@gmail.com